

A I D S TREATMENT N E W S

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Now you can follow treatment news as it happens at AIDSNEW, a free service of *AIDS Treatment News*. We select quality reports in medical journals, AIDS treatment sites, and the general press, and publish Web links to them at www.connotea.org/group/aidsnew -- all in one place, often on the first day the news is available anywhere. No need to subscribe, register, or log in. Just visit www.connotea.org/group/aidsnew, scroll down, and click any of the titles for more information. You can use almost any computer and Web browser.

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Large doses of resveratrol (found in small amounts in red wine) made headlines recently for extending the lifespan of mice on an unhealthy diet. This and other substances found in some wines and foods may protect against cardiovascular disease or diabetes, and improve the functioning of mitochondria in cells (which could reduce certain adverse effects of HIV and the drugs used to treat it).

**Lung Cancer: Very High Death Rate with HIV, Huge Reduction Possible with CT Screening for Early Diagnosis.....
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Lung cancer has a high death rate, especially with HIV in one group of patients studied recently. Researchers are finding that most of the fatalities are due to late diagnosis; as many as 80% of the deaths from lung cancer in the general population might be prevented by CT screening to find the tumors early. The patients with HIV were often relatively healthy, so doctors did not suspect that they had cancer.

AIDS Treatment News

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Statement of Purpose:

AIDS Treatment News reports on experimental and standard treatments, especially those available now. We interview physicians, scientists, other health professionals, and persons with AIDS or HIV; we also collect information from meetings and conferences, medical journals, and computer databases. Long-term survivors have usually tried many different treatments, and found combinations that work for them. *AIDS Treatment News* does not recommend particular therapies, but seeks to increase the options available.

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U.S. Guidelines: Adult/Adolescent Revision Published October 10, 2006; Perinatal October 12; Pediatric October 26.....

Three U.S. HIV treatment guidelines were revised in October.

AIDSNEW Treatment Alerts: Appendix.....

Here are details on our AIDSNEW service (see first article, above) that most users will not need to know.

[Note: Though dated October, this issue went to the printer on 2006-12-15.]

Daily News Alerts Selected by *AIDS Treatment News*: www.connotea.org/group/aidsnew

by John S. James

AIDS Treatment News now provides a service where you can read key treatment and related news as it happens, all in one place. We select from medical journals, AIDS treatment Web sites, online newspapers, and many other Web pages that come to our attention -- so that you can check important treatment news quickly, at your convenience. This service, called AIDSNEW, is free for everybody, with no subscription, registration, or signup required. It should work with almost any computer and software that can browse the Web.

To try it, visit www.connotea.org/group/aidsnew

Scroll down, and in the center column you will find Web links to the stories we selected, beginning with the ones we added most recently. Each has a title; many but not all have a brief comment or quote added by *AIDS Treatment News* (in grey text). If you want more information, click the title to get a free abstract (and full text of the document as well, if it is free online). The

information is usually authoritative because it comes from the original source, a peer-reviewed journal or other publication we believe to be reliable.

AIDS Treatment News selects an average of several news alerts per day. And we go to some trouble to provide a smooth user experience -- finding quality news that is free to nonsubscribers of the journal or newspaper (or at least has a meaningful free abstract). A few of the Web pages we link to do require free registration -- but more than 90% do not. Some of the headlines and articles are more technical than *AIDS Treatment News*, because they were written mainly for doctors. Just skip them if necessary,

You can keep up with major HIV/AIDS treatment-related news by spending about ten minutes a week to scan the headlines, plus the time to read any of these reports in depth. Local or national communities can be informed rapidly by this service and others like it -- and have the same information in common, so they can act immediately if needed. Also, important research will better reach those who want to know, and not get lost in the flood of routine information.

Look and Feel

We are providing this service using software called Connotea (pronounced Conn-o-te'a), created and made available free by Nature Publishing Group (which publishes *Nature*, *Nature Medicine*, and over five dozen other scientific journals). This software also lets you search annotated Web links (called "bookmarks" in Connotea) contributed publicly by hundreds of scientists and doctors. The page at www.connotea.org/group/aidsnew may look busy; but if you only want to follow our news service you can ignore everything except our alerts, in the center column starting near the bottom of the screen. We cannot change the format of the page.

We could have changed the inconsistent capitalization of titles, but instead chose to leave the capitalization style that was used in the original articles.

1. This kind of news distribution can sometimes publish page-one stories even before the Web sites of major TV networks or other news organizations. For example, the recent report on adult male circumcision was released by NIAID (a branch of the U.S. National Institutes of Health), apparently to everyone simultaneously; our copy was sent at 19 seconds after noon on December 13. We checked email a few minutes later, and needed about five minutes to read and publish the story, by linking to the definitive NIAID site.

2. Despite its speed, this publication system includes human judgment, with every alert personally selected for the specific audience.

3. *AIDS Treatment News* spent no money at all on this project (\$0.00) -- and little time beyond keeping up with the news, which we need to do anyway. Others could easily publish a similar service based on their own expertise -- likely providing the best (or the only) news feed anywhere in their areas of interest. AIDS-related topics might include access issues, prevention, U.S. or U.N. agencies, political action alerts, fundraising, immunology, pathogenesis, drug effects and choices, or dozens of other focus areas.

4. If you want us to consider using your news release in the AIDSNEW alert service, you must publish it on the Web, not just send it in email (this is for technical reasons, not policy). You could easily publish your news on a blog, and then send an email announcement telling people where it is. Remember that our readers will not see your email, only what you put on the Web.

For More Information:

1. Try our news-alert service at www.connotea.org/group/aidsnew
2. For technical details, including which journals we follow most closely, or using RSS, see "AIDSNEW Treatment Alerts: Appendix" in this issue.
3. To learn more about Connotea see "AIDS Information Overload: What You Can Do Now," in *AIDS Treatment News* #419. Or in Connotea, see the 'Beginner's guide' links on the bottom of every page.

You have our permission to send this announcement to others who may be interested.

Resveratrol:

Notes for Organizations:

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800-TREAT-1-2

Why It Matters in HIV

by John S. James

"Resveratrol extends the lifespan of every species we have fed it to. We are now showing that this is also possible for mice on a high-fat diet." David Sinclair, Harvard Medical School and Sirtris Pharmaceuticals (<http://www.sirtrispharma.com/>), a company he co-founded to commercialize resveratrol-related discoveries.

The headline stories in November 2006 about an ingredient in red wine, chocolate, and some other foods improving the health and extending the lifespan of mice fed a high-fat diet did not involve HIV -- yet we need to pay attention. In animal studies, resveratrol and related substances have many effects that may reduce diabetes, cardiovascular disease, and mitochondrial damage in cells (a likely cause of many cases of neuropathy, as well as other problems), and significantly increase healthy lifespan.

No human trials have been done -- and it would be impossible to get the same dose of resveratrol from red wine, for example, as was given to mice in the recent test. No one knows what dose would be needed for human benefit, as no such benefit has yet been proved (because testing in humans is much more difficult than in mice). So far resveratrol has helped animals, and at least one company is trying to change the natural molecule to optimize its use as a patented human drug.

How is this relevant to HIV? See our "Comment on HIV..." below.

Recent Articles

Here are some places to check for more information, as of early December 2006:

* On October 31, 2006, a day before the scientific publication of the benefit of resveratrol in mice, *The New York Times* published an article about calorie restriction in monkeys. [1] It has been

known since 1935 that animals fed a complete diet but with about 30% or 40% fewer calories will stay healthy and live longer than animals fed their usual diet. Some scientists believe that this effect evolved as a mechanism to help animals and people survive famine -- and that resveratrol works by stimulating the same genetic mechanism.

* A day later (November 1), the science journal *Nature* published online a key study in mice [2] -- and *The New York Times* provided a non-technical description [3], as did *Forbes* [4]. At one year of age (middle age for a mouse), mice were started on an unhealthy high-fat diet (about 60% of their calories from fat); others stayed on their usual laboratory diet. Some of the mice on the high-fat diet were also given resveratrol. They did get fat, but remained healthy like the normally fed mice, and lived as long. The animals fed the high fat without resveratrol showed signs of diabetes and died months earlier.

* On November 15, the biology journal *Cell* published a finding that resveratrol improved mitochondrial function and protected against metabolic disease (often a precursor of diabetes) in mice. [5]

* On November 30, *Nature* reported a finding that other ingredients in red wine, procyanidins (not resveratrol, because the amount present is too small), were the "principal vasoactive polyphenols" in red wine -- and were highest in regions where wine was prepared by traditional methods that extracted these compounds efficiently from the grapes. The paper noted that people in these regions tended to live longer. [6]

* In early December, *Antioxidants and Redox Signaling* published findings on how resveratrol may help protect the heart. [7]

Additional resveratrol background was compiled by the Linus Pauling Institute. [8] But as we go to press, that document was last updated in March 2005, so it does not include the recent work.

Various products containing resveratrol

(and other products with procyanidins) have been sold for some time as food supplements. We have no information on their quality.

The Linus Pauling Institute background paper noted that resveratrol had been reported to inhibit the liver enzyme cytochrome P450 3A4 (also called CYP3A4), though this had not yet been tested in humans. If it does so it would increase blood levels of drugs metabolized by that enzyme; for some drugs the increase could be dangerous. [8] Grapefruit juice also inhibits the same enzyme -- so if one has been cautioned to avoid grapefruit juice because of interaction with prescription drugs, one might be cautious with resveratrol as well.

Many doctors and scientists say it is too early to rush to take large doses of resveratrol supplements of uncertain quality. Some are taking it themselves, however.

Comment re HIV: Studies We Need Now, and Why We Are Unlikely to Get Them

Earlier, some researchers looked at resveratrol as a possible HIV treatment -- although we have not seen any papers published on this since 2004. (To check what has been published in peer-reviewed journals and read the abstracts, visit <http://www.pubmed.gov> and enter "resveratrol hiv" without the quotation marks into the search bar near the top of the window, then click Go).

Today we would most want to see small trials to find out if resveratrol might help relieve certain drug side effects, or other problems resulting from HIV disease -- including lipid or other metabolic abnormalities, or neuropathy, or other symptoms suspected of being caused by mitochondrial damage. Trials aiming to relieve symptoms, or normalize blood levels that are easily measured, could

potentially get results fairly quickly and with a fairly small number of volunteers. This is because a measurement is always available, avoiding the need to wait for rare "events" like disease progression or death, for end-point data to be collected.

The main problem in organizing such trials is that there is little economic incentive, unless the goal is to develop a costly, proprietary drug (requiring lots of bureaucracy and generating years of delay). Today greed is usually the *sine qua non* of drug development within the U.S. and multinational corporate system, and this system imposes its standards on the world. Greed in medicine is prone to intolerable abuses (when companies or individuals sacrifice the health of thousands of people for the promise of more profit for themselves). Therefore it requires heavy-handed controls, which cause major administrative delays and other lost opportunities, delays and losses that are not medically or scientifically necessary. We need alternative drug development systems. But institutional abuses (such as patents on human biology [9]) make alternatives difficult.

References

Note: All of the following except [1] and [9] (which do not mention resveratrol) can be found at www.connotea.org/group/aidsnew; type "resveratrol" in the 'Search' bar, and click 'Find results'.

1. One for the Ages: A Prescription That May Extend Life. Michael Mason, *New York Times*, October 31, 2006; <http://www.nytimes.com/2006/10/31/health/nutrition/31agin.html> (registration required).

2. Baur JA, Pearson KJ, Price NL, and others. Resveratrol improves health and survival of mice on a high-calorie diet. *Nature*, November 16, 2006; volume 444, pages 337-342 (published electronically November 1).

3. Yes, Red Wine Holds Answer. Check Dosage. Nicholas Wade, *New York Times*, November 2, 2006; <http://www.nytimes.com/2006/11/02/science/02drug.html> (registration required).

4. Compound in Red Wine Boosts Health of Obese Mice, *Forbes*;

<http://www.forbes.com/forbeslife/health/feeds/hscout/2006/11/01/hscout535859.html> (you may need to wait for an ad).

5. Lagouge M, Argmann C, Gerhart-Hines Z, and others. Resveratrol Improves Mitochondrial Function and Protects against Metabolic Disease by Activating SIRT1 and PGC-1alpha. *Cell*; published ahead of print November 15.

6. Corder R, Mullen W, Khan NQ, and others. Oenology: red wine procyanidins and vascular health. *Nature*; November 30, 2006, volume 444, page 566.

7. Goh SS, Woodman OL, Pepe S, Cao AH, Qin C, and Ritchie RH. The red wine antioxidant resveratrol prevents cardiomyocyte injury following ischemia-reperfusion via multiple sites and mechanisms. *Antioxidants and Redox Signaling*, January 2009; volume 9, number 1, pages 101-103.

8. Higdon J and Steward WP. Resveratrol. (2005-03-04) Linus Pauling Institute at Oregon State University. <http://lpi.oregonstate.edu/infocenter/phytochemicals/resveratrol/>

9. "Astonishingly, the Federal Circuit also held that physicians (or researchers) would infringe the patent merely by thinking about the relation between homocysteine and vitamin deficiency when they analyzed an alternative homocysteine test." From "When Patents Threaten Science," *Science*, December 1, 2006. What was patented was to use any test to measure the amino acid homocysteine, and conclude from a high level that a vitamin B deficiency was likely. (Excessive homocysteine may be a serious risk factor for heart attack, stroke, and other cardiovascular disease -- although as of November 2006 it is not

officially recognized as such in the U.S. standard of care). LabCorp was ruled liable for over \$2,000,000 damages for selling its own homocysteine test -- and the U.S. Supreme Court dismissed the appeal, leaving the ruling standing as U.S. law.

There are many other patent-abuse examples. For a short explanation of what went wrong recently in the U.S. patent system, see "The Patent Trap," *Harvard Magazine*, July-August 2005, <http://www.harvardmagazine.com/online/070575.html>

This article reviews the book *Innovation and Its Discontents: How Our Broken Patent System Is Endangering Innovation and Progress and What to Do about It* (published 2005), by Josh Lerner and Adam B. Jaffe, professor of investment banking at Harvard Business School and professor of economics at Brandeis, respectively.

Lung Cancer: High Death Rate with HIV, Huge Reduction Possible with CT Screening for Early Diagnosis

by John S. James

Lung cancer causes more deaths than any other kind of cancer in both men and women. It is especially fatal with HIV, in large part due to late diagnosis. Recently a major study found that in the general population, annual low-dose CT scans (formerly called CAT scans) could reduce U.S. lung-cancer deaths probably by 80% through early diagnosis. Clearly the public should note this option for doing better in saving lives.

HIV and Lung Cancer

A study of medical records at Johns Hopkins Hospital found 92 patients who had HIV and were diagnosed with lung cancer at the hospital. [1] Ninety two percent of them died of lung cancer -- a 57% increase over the death rate for HIV-negative patients.

Most of the deaths were due to late diagnosis. In 32 patients in the Johns

Hopkins HIV clinic, 60% of standard chest X-rays found no evidence of cancer within one year of diagnosis -- compared to only 4% of chest CT scans (1 in 28 scans missed the diagnosis).

Lung-cancer patients were often young, and with their HIV disease well controlled -- so doctors were unlikely to suspect lung cancer. Their median survival was only six months after diagnosis, even after the introduction of HAART.

Other studies had found that HIV patients had three to eight times the lung-cancer risk of the general population. [1]

Better Diagnosis by CT Scans

In the general population the five-year survival rate is 70% if lung cancer is caught at stage I (localized cancer), but only 5% at stage IV (distant metastases). Stage I diagnosis is unusual, mainly by lucky accident, so the overall survival rate is low.

Two months after publication of the HIV study above, the *New England Journal of Medicine* published results from screening over 31,000 patients annually (about two thirds of them in the U.S.) with a low-dose CT scan, using a diagnosis and treatment protocol designed for this study. [2,3] The screening diagnosed lung cancer in 484 of the participants -- 85% of them in stage I. For those in stage I, the estimated 10-year survival rate was 88% -- 92% for those who had surgery within one month of diagnosis. Eight of the patients diagnosed with stage I lung cancer did not get treatment, and all of them died within five years.

Comment

Smoking causes 87% of lung cancer, according to the American Lung Association ("Facts About Lung Cancer," November 2006), and quitting smoking lowers one's risk each year. Avoiding smoking and better diagnosis are both essential to controlling this huge cause of death.

Note that a new prescription drug, CHANTIX (varenicline), has been approved

to help people quit. An editorial on this drug in the November 2006 *Annals of Internal Medicine* noted that even a small increase in smoking quit rates would be more important than any other medical intervention.

References

[1] Brock MV, Hooker CM, Engels EA, and others. Delayed diagnosis and elevated mortality in an urban population with HIV and lung cancer: Implications for patient care. *Journal of Acquired Immune Deficiency Syndromes*. September 2006; volume 43, number 1, pages 47-55.

[2] Henschke CI, Yankelevitz DF, Libby DM, and others. Survival of patients with stage I lung cancer detected on CT screening. *New England Journal of Medicine*. October 26, 2006; volume 355, number 17, pages 1763-1771.

[3] Unger MD. A pause, progress, and reassessment in lung cancer screening [editorial]. *New England Journal of Medicine*. October 26, 2006; volume 355, number 17, pages 1822-1824.

U.S. Guidelines: Adult/Adolescent Revision Published October 10, 2006; Perinatal Guidelines October 12; Pediatric Guidelines October 26

Revised *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents* were issued October 10 to take advantage of new drug information from clinical trials. A one-page summary of the changes is included on the second page of the document. Changes from the previous version are highlighted in yellow.

Also, new perinatal guidelines for antiretroviral treatment for maternal health, and to prevent mother-to-child transmission of HIV, were published two days later, October 12. New pediatric

treatment guidelines were published October 26.

To download the latest official U.S. AIDS-related guidelines, these and others, visit <http://www.aidsinfo.nih.gov/guidelines/>. Select the guidelines you want in the menu on the left, and click to download either the PDF version, or a PDA version (Portable Digital Assistant), a stripped-down PDF file designed for easier viewing on a handheld device.

AIDSNEW Treatment Alerts: Appendix

This is a technical appendix to "Daily News Alerts Selected by *AIDS Treatment News*: www.connotea.org/group/aidsnew" (in this issue).

What Medical Journals and Other Sites Do We Cover?

We focus on research reports in medical journals including:

AIDS
Annals of Internal Medicine
British Medical Journal
Clinical Infectious Diseases
JAIDS (Journal of Acquired Immune Deficiency Syndromes)
HIV Medicine
JAMA
Journal of the Association of Nurses in AIDS Care
Journal of Infectious Diseases
The Lancet
MMWR
Nature Medicine
New England Journal of Medicine
PLOS Medicine (Public Library of Science)
Science
any other journals when we see important research;
also, presentations at conferences.

We include articles published on AIDS sites, for example:

AEGIS, <http://www.aegis.org>
AIDSmeds.com,
<http://www.aidsmeds.com>
AIDSmap.com, <http://www.aidsmap.com>
HIV Treatment Bulletin (iBase),
<http://www.i-base.org.uk/htb/>
The Body, <http://www.thebody.com>
HIVandHepatitis.com,
<http://www.hivandhepatitis.com>
Kaiser Daily HIV/AIDS Report,
http://www.kaisernetwork.org/daily_reports/rep_hiv.cfm
NATAP, <http://www.natap.org>
Clinical Care Options for HIV,
<http://www.ClinicalOptions.com/hiv>
POZ, <http://www.poz.com>
TAG, <http://www.aidsinfonyc.org/tag/>
We also include other AIDS sites, and some online newspaper articles if they do not require registration.

Receiving Our Alerts in RSS

If you use an RSS reader, you can subscribe to our alert service and receive our alerts.

Unless you are already using RSS, it provides little advantage in using the AIDSNEW alert service. RSS is good for following many different blogs or other news sources simultaneously. If you are using only a few news sources, RSS is unnecessary.

Searching, AIDSNEW, and Connotea

You do not need to do any searching on AIDSNEW, since its main purpose is to supply recent news you may never have heard of (and therefore cannot search for) -- not to provide an archival database of news.

But you can use Connotea to search for bookmarks (Web links) contributed by many scientists and doctors, not just us. For example, *AIDS Treatment News* added fewer than 300 bookmarks (Web links to news) to AIDSNEW before announcing this service.